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REVIEW

Age- and Sex-Specific Burden of Cardiovascular Disease Attributable to 5 Major and Modifiable Risk Factors in 10 Asian Countries of the Western Pacific Region

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Cardiovascular disease (CVD) is the leading cause of mortality worldwide, causing an estimated 18 million deaths annually. Much of the burden of CVD resides in lower- and middle-income countries, particularly those Asian countries comprising the Western Pacific Region. Epidemiological studies have convincingly shown that up to 90% of all CVD can be explained by a small number of modifiable risk factors, including blood pressure, smoking, diabetes, total cholesterol and excess body weight. However, the relationship between these risk factors and coronary artery disease and stroke often differ by age and sex, and yet these differences are often overlooked in burden of disease estimations. As such, that can result in either an over- or under-estimation of the disease burden in specific population subgroups, which may affect resource allocation of healthcare. In this review, we derive the most reliable and previously unpublished estimates of the age- and sex-specific burden of vascular disease attributable to the aforementioned risk factors for 10 of the most populous Asian countries in the Western Pacific Region. Understanding how the burden of vascular disease is distributed within and between populations is crucial for developing appropriate health policies and effective treatment strategies, particularly in resource-poor settings. (*Circ J* 2015; **79:** 1662–1674)

Key Words: Blood pressure; Cholesterol; Coronary risk factors; Smoking; Stroke

Globally, cardiovascular disease (CVD) remains the leading cause of mortality, causing an estimated 18 million deaths (≈one-third all deaths) each year from coronary artery disease (CAD) and stroke.[1] Once considered to be a Western disease, CVD has swiftly made steep inroads into many lower- and middle-income countries as they attain increasingly greater levels of economic and social development.[2] Consequently, CVD is responsible for an already significant and growing burden of death and disability in these countries; indeed, recent estimates suggest that up to 80% of all CVD deaths now occur in lower- and middle-income countries, particularly in Asia.[1] As such, it may be more appropriate to consider CVD as a "disease of development" rather than a "disease of affluence".[2] China is perhaps the most obvious, and perhaps important example, of an economically developing country in Asia where the pattern of mortality has transitioned from being one dominated by communicable diseases in the mid-20th century to one where mortality from CVD and cancer are now preeminent (**Table S1**).[3]

The primary reasons for why Asian countries in particular are shouldering the greatest burden of CVD are largely sociodemographic in origin. Compared with the rest of the world, these countries constitute some of the largest populations; China, India and Indonesia alone represent 40% of the global population (≈2.9 billion people). Another shared commonality is that Asian countries (with the clear exception of Japan) have relatively young populations who are, despite their relative youth, already experiencing levels of cardiovascular risk factors that are more commonly observed in older individuals. Indeed, the proportion of deaths due to CVD risk factors in people less than 60 years of age is higher in populations in lower- and middle-income countries compared with high-income countries.[4]

A less-obvious ramification of having a high prevalence of risk factors such as diabetes mellitus (DM) in a relatively young population is that the effect of diabetes and other vascular risk

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factors such as blood pressure (BP) on vascular risk is far stronger at younger than older ages. With respect to BP, this was definitively demonstrated by the Prospective Studies Collaboration in a landmark paper examining the relationship between BP and vascular disease: among individuals 40–49 years, a 20 mmHg lower systolic BP was associated with 64% reduction in the risk of stroke death and a 51% lower mortality from ischemic heart disease. In comparison, at ages 70–79 years the corresponding estimates were significantly lower at 50% and 40%, respectively. Finally, coinciding with increased economic development has been a marked shift in the proportion of the Asian population from traditional, agrarian lifestyles to more urbanized environments and with it, the adoption of more adverse behavior patterns such as reduced levels of activity, deterioration in the quality of diet, and increased exposure to a plethora of other known vascular risk factors.[5–7]

Major and Modifiable Risk Factors for CVD

Largely as a result of large-scale epidemiological studies, more than 90% of all cardiovascular events can be attributed to a relatively small number of modifiable risk factors, chiefly BP, cigarette smoking, lipids, type 2 DM and excess body weight.[8] Elevated BP and smoking alone have been estimated to explain more than 1 in every 5 deaths globally (or 12.6 million deaths annually).[9] The large case-control studies INTERHEART[10] and INTERSTROKE[11] have elegantly illustrated the contribution of 9 modifiable risk factors (in addition to those listed above, include psychosocial health, exercise, alcohol and diet) to major vascular disease. Moreover, those studies highlighted the substantial geographical variation in the attributable burden of vascular disease due to particular risk factors. For example, in Western Europe, North America and South East Asia, the burden of myocardial infarction attributable to obesity (which is highly prevalent in these regions) exceeded that due to smoking (which is less common), whereas the converse was found in China, which has a comparatively low prevalence of obesity but high male smoking rates. However, the case-control study design of these studies is suboptimal for etiological research and furthermore the study populations were highly-selected and unrepresentative of the general population. Calculation of the "true" disease burden requires population-based studies that are able to more reliably quantify the associations between exposure and disease outcome.

Past estimations of the burden of vascular disease have largely ignored the changing distribution of the prevalence of risk factors with age and sex. There has also been a general lack of consideration given to the attenuation of the relationship between some risk factors and age.[12,13] Similarly, some risk factors such as diabetes and smoking have been shown to confer a greater excess vascular risk in women relative to men, yet these age and sex differences in the relationships between risk factors and outcomes are rarely taken into account in burden of disease estimates.[14,15] Consequently, past estimates can give the misleading impression that the burden of CVD for a specific population is uniform across age and sex groups, when in reality it can vary substantially.

In this review, we undertook a comparative analysis of the age- and sex-specific prevalence of 5 leading major vascular risk factors, namely BP, cigarette smoking, body mass index (BMI), diabetes (DM) and total cholesterol (TC) for 10 of the most populous Asian countries of the World Health Organization Western Pacific Region using nationally representative and contemporary studies.[16] Without exception, all of these countries have a substantive burden of CVD (**Figure S1**); however, considerable variation in the causes and distribution of vascular disease exists both within and between these countries. For the purposes of this review and to facilitate meaningful inter-country comparisons, we excluded the largely non-Asian populations of Australia and New Zealand from further analysis.

Derivation of the Population-Attributable Fractions (PAF) for CAD and Stroke

Nationally representative data on the age- and sex-specific prevalence for the 5 vascular risk factors (hypertension, smoking, overweight and obesity, diabetes and hypercholesterolemia) were obtained for Cambodia,[17] China,[18] Japan,[19] Malaysia,[17] Myanmar,[17] People's Republic of Lao,[17,20] Singapore,[21] Thailand,[17] The Philippines,[22] and Vietnam[23] through a review of published national data, including web pages, and through personal contacts (**Table S2**). Smoking was defined by self-report questionnaire in all surveys; hypertension was defined as BP ≥140/90 mmHg in The Philippines, or in combination with (1) current medication usage in Japan, Cambodia, Myanmar, Singapore, Vietnam and Laos or (2) with a previous diagnosis by a physician in China, or with both (1) and (2) in Malaysia and Thailand; elevated TC was defined as ≥6.2 mmol/L (except in Malaysia, which used a cut-point of 5.2 mmol/L); excess body weight was defined as BMI ≥25 kg/m² (except in China, which used 24 kg/m² as the cut-point). The diagnosis of DM varied among the countries (**Appendix**). Estimates of the variance around the prevalence estimates were not available from the published reports, which precluded the calculation of a measure of uncertainty around the point prevalence estimates.

The outcome analyzed in this study was the population-attributable risk, calculated as:

$$\frac{pE(\lambda-1)}{1+pE(\lambda-1)}$$

where p_E is the probability of exposure to the risk factor (ie, the population prevalence) and λ is the relative risk for those exposed to the risk factor vs. those unexposed.[24] For each of the 5 risk factors, across selected countries, we derived values of pE by age and sex group. For each risk factor, we estimated age-adjusted values of λ using Asian data from the Asia Pacific Cohort Studies Collaboration (APCSC).[25] Asian data from the APCSC are derived from mainland China (16 studies; 261,000 people), Japan (12; 35,000), Hong Kong (1; 3,000), Taiwan (2; 8,500), Thailand (1; 3,500), Singapore (2; 5,600), South Korea (1; 184,000), giving a total of almost 500,000 subjects.[26] For each country and each risk factor, age group/sex-specific estimates were estimated from Cox proportional hazard models, stratified by study, where age, sex, the risk factor and their interactions were included as covariates. Age was fitted as a continuous variable and each age group effect estimated at the mid-range of the age group. The age groups used, and the definition used for the risk factor exposure, were taken so as to correspond with the published data on the respective risk factor. For both sexes, once all the age group-specific risk factors were available for any one country, an overall sex-specific population-attributable risk was derived for that country by weighting the age group-specific results by the population distribution according to published sources.

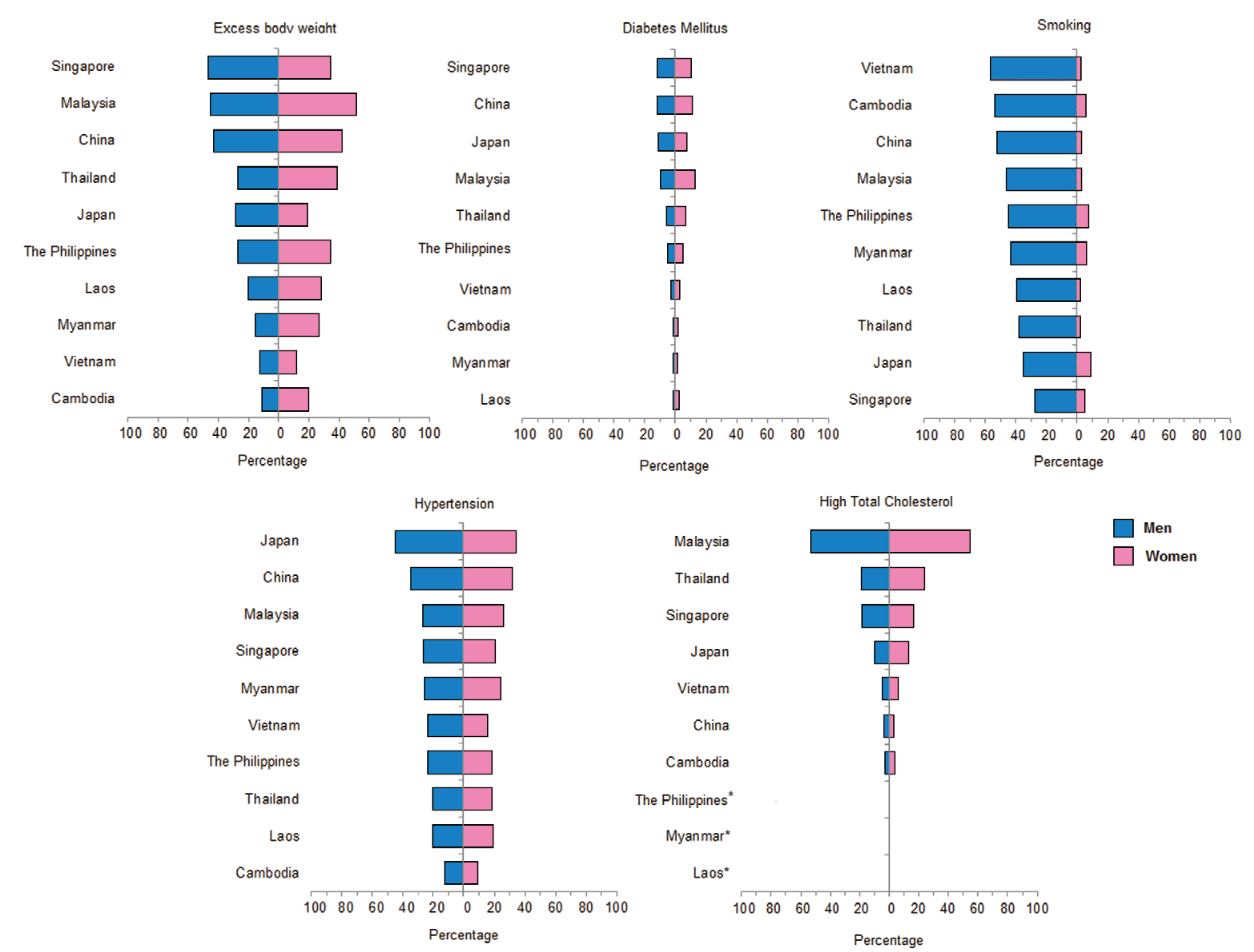

Figure 1. Prevalence of 5 major risk factors for coronary artery disease separately in men and women for selected Asian countries of the Western Pacific Region. *Information not available.

Age- and Sex-Specific Burden of CAD and Stroke Attributable to Major and Modifiable Risk Factors in the Western Pacific Region

Hypertension

The overall age-adjusted prevalence of hypertension varied substantially among the 10 countries in both women and men (**Figure 1**). Cambodia had the lowest prevalence, at roughly 13% in men and 10% in women, while the corresponding estimates in Japan were 4-fold greater: 55% in men and 40% in women. These data mask the considerable age-related increase in the prevalence of hypertension that was apparent in all of the countries, irrespective of the level of economic development, and in both sexes (**Table 1**). Japan and China represented the most extreme examples of this; in Japanese men aged 20–29 years the prevalence of hypertension was approximately 7%, increasing by more than 10-fold to 75% in those aged over 70 years. In Japanese women, the age difference was even more extreme, with an estimated prevalence of less than 1% in 20–29-year-olds to more than 73% in those aged over 70 years. In the 3 least-economically developed countries, Myanmar, Laos and Cambodia, the age-related increase in the prevalence of hypertension was also evident in women and men but to a lesser extent than in Japan and China. For example, in Vietnam the prevalence in men increased from approximately 12% in those aged 25–34 years to 45% in those aged 55–64 years. In women, the corresponding estimates were 5% and 37%, respectively.

Given the aforementioned variation in the sex- and age-specific prevalence of hypertension between countries, as well as marked differences in the age-structure of their respective populations, it is not surprising that the attributable disease burden for hypertension should summarily reflect this variation. In men, for CAD the greatest attributable burden due to hypertension was in Myanmar (35%) and China (34%), and least in Cambodia (18%) and Thailand (21%) (**Figure 2**). In women, The Philippines (26%) and Japan (23%) had the greatest attributable burden of CAD due to hypertension, whereas Cambodia (9%) and Vietnam (13%) had the smallest burden. As the prevalence of hypertension increased across successive age groups, the attributable burden of CAD due to hypertension also tended to increase with age in both women and men and in most countries, but to a lesser extent due to the substantial age attenuation in the strength of the association between BP and both CAD and stroke.

The strength of the relationship between BP and risk of

Table 1. Age- and Sex-Stratified Prevalence of Hypertension and the PAF (%) of CAD and Stroke Across Selected Countries From the Western Pacific Region

Age group (years)	Men			Women		
	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)
Thailand						
15–29	4.61	36.03	14.63	0.88	3.25	0.82
30–44	15.35	50.34	25.69	10.09	21.82	8.94
45–59	28.19	48.77	25.95	30.55	37.20	23.56
60+	47.10	37.18	17.05	48.95	36.67	34.02
Japan						
20–29	7.30	44.14	19.78	0.70	2.45	0.66
30–39	22.20	61.46	34.92	3.50	9.19	3.28
40–49	32.30	60.10	35.01	12.60	22.46	11.11
50–59	57.30	62.59	38.28	33.50	37.58	25.40
60–69	65.20	52.75	28.97	52.80	41.99	35.47
70+	75.50	39.84	16.88	73.30	42.53	43.86
Malaysia						
25–34	10.50	48.13	23.14	10.40	25.13	9.05
35–44	23.70	57.92	32.37	19.20	33.16	15.84
45–54	37.20	58.00	33.55	40.30	45.09	28.81
55–64	58.10	56.77	32.80	54.20	46.05	35.79
Cambodia						
25–34	6.10	35.03	14.89	2.30	6.91	2.15
35–44	11.90	40.87	19.37	8.20	17.48	7.44
45–54	17.90	39.92	19.54	16.00	24.59	13.84
55–64	26.60	37.55	18.26	22.00	25.73	18.45
Myanmar						
15–24	14.40	65.55	36.28	8.00	24.18	6.95
25–34	18.10	61.53	34.17	14.80	32.33	12.40
35–44	31.80	64.88	39.10	28.50	42.41	21.84
45–54	37.10	57.93	33.49	39.70	44.72	28.50
55–64	51.00	53.55	29.99	53.20	45.59	35.37
Singapore						
30–39	10.90	43.92	20.85	4.50	11.52	4.18
40–49	21.90	50.53	26.75	11.50	20.91	10.24
50–59	33.10	49.14	26.38	30.80	35.63	23.84
60–69	53.80	47.95	25.18	53.00	42.08	35.55
The Philippines						
20–29	11.40	41.40	27.19	3.70	22.33	15.57
30–39	19.80	47.72	31.26	11.60	38.61	29.04
40–49	27.20	47.84	29.54	22.70	45.66	35.52
50–59	36.70	46.91	26.04	33.80	45.22	35.00
60–69	41.60	40.79	17.52	40.30	37.99	27.95
70+	43.50	31.76	6.68	43.30	26.80	17.36
China						
18–24	12.20	60.78	31.86	7.00	21.47	6.14
25–34	20.40	64.32	36.91	10.60	25.49	9.21
35–44	30.90	64.22	38.42	22.30	36.55	17.94
45–54	42.40	61.15	36.52	41.70	45.94	29.52
55–64	55.60	55.69	31.83	58.60	48.00	37.61
65–74	67.20	45.78	22.67	70.00	45.29	42.44
75+	71.40	28.62	7.97	73.90	38.59	44.34
Vietnam						
25–34	11.90	51.26	25.44	4.50	12.68	4.13
35–44	20.90	54.83	29.68	12.90	25.00	11.23
45–54	33.10	55.13	30.99	22.70	31.63	18.56
55–64	45.20	50.54	27.52	37.20	36.94	27.67
Laos						
25–34	8.90	44.03	20.33	12.90	29.40	10.98
35–44	17.80	50.83	26.44	17.10	30.64	14.36
45–54	30.80	53.34	29.47	22.40	31.34	18.36
55–64	45.30	50.59	27.56	41.50	39.53	29.92

CAD, coronary artery disease; PAF, population-attributable fractions.

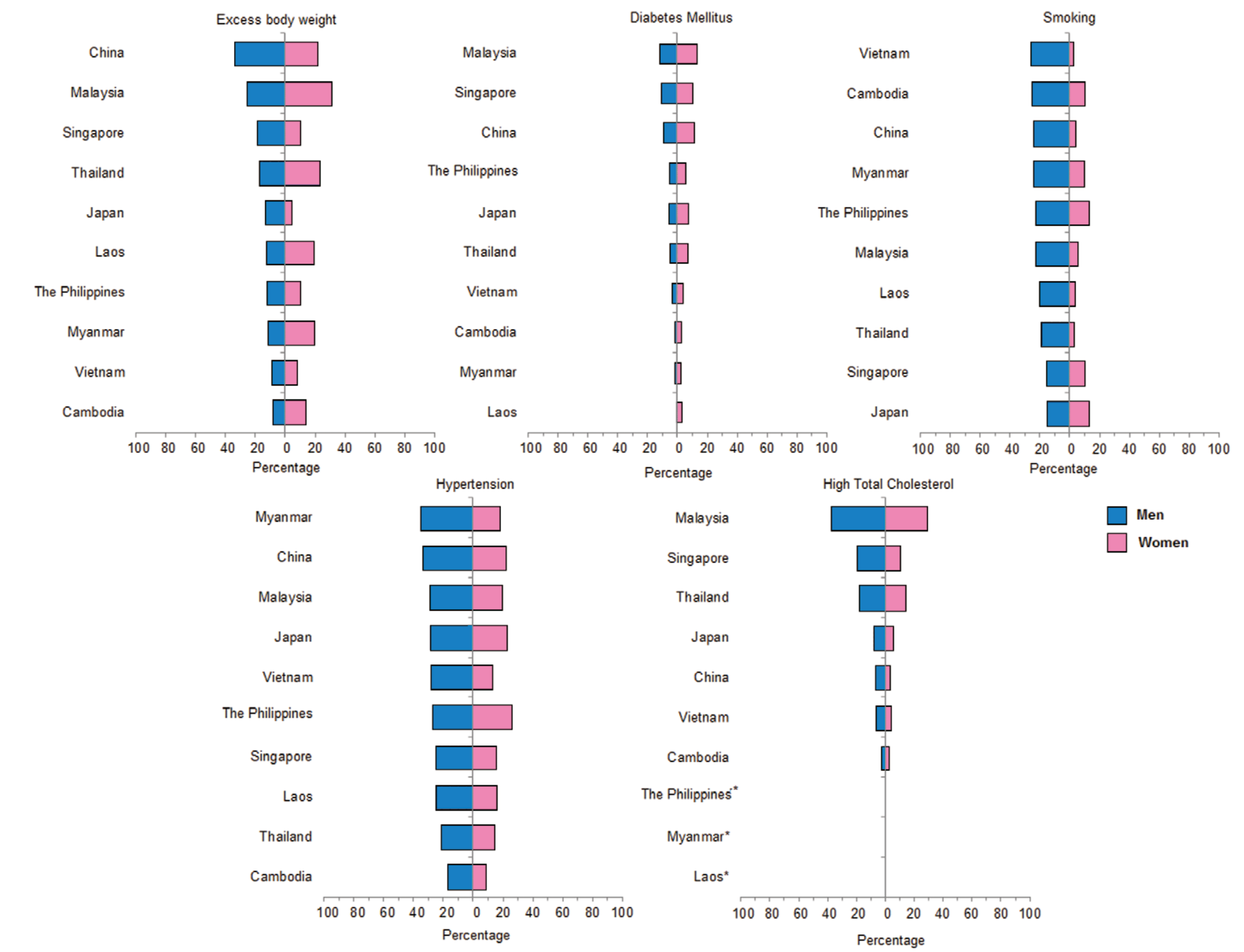

Figure 2. Population-attributable fraction (%) of coronary artery disease explained by individual risk factors separately in men and women from selected Asian countries of the Western Pacific Region. *Information not available.

stroke is markedly stronger than with CAD at all ages and in both sexes, hence the PAF estimates for stroke attributable to hypertension were substantially larger than those observed for CAD (Figure 3). Thus, hypertension explained roughly 60% of all stroke events in men in Myanmar and China, down to approximately 40% in Cambodia and Thailand. In women, hypertension explained more than one-third of all strokes in China, Myanmar, Malaysia, The Philippines, and Laos, and approximately one-quarter of all strokes in the remaining countries (with the exception of Cambodia where only 17% of all strokes were explained by hypertension).

Cigarette Smoking

There is little doubt that across much of the Western Pacific Region cigarette smoking is endemic among men, but in stark contrast remains relatively uncommon among women (Figure 1).[27] In men, the highest smoking prevalence rates are observed in the least-economically developed countries in the region such as Vietnam, Cambodia and China (age-standardized prevalence rates >50%) and vice versa: the most developed countries led by Singapore had the lowest prevalence of smoking in men (30%). As with hypertension, considerable differences in the country-specific age-related trends in smoking existed (Table 2). For example, in the least-developed countries such as Cambodia and Vietnam the prevalence of smoking in men can be seen to increase successively across age groups. By comparison, in Japan and Singapore, there is no evidence of higher prevalence rates with successive age groups, rather the opposite, in that smoking prevalence rates tend to decline in men older than 50 years. A plausible explanation for this trend is that among middle-aged men smoking cessation is uncommon in the least developed compared with the most developed countries for a raft of reasons, including the latter having more stringent tobacco control policies, greater population awareness of the hazards of smoking, and more effective smoking cessation campaigns.

Largely due to cultural barriers smoking in women has been, and continues to remain, a relatively uncommon occurrence in Asian populations despite huge efforts by "big tobacco" to reverse this situation.[28] Age-standardized prevalence estimates ranged from 2% in Thailand to 16% in The Philippines. In China, the corresponding estimate was 2.5% (compared with 53% in men). Similar to men, for the most economically developed countries such as Singapore and Japan, age-specific

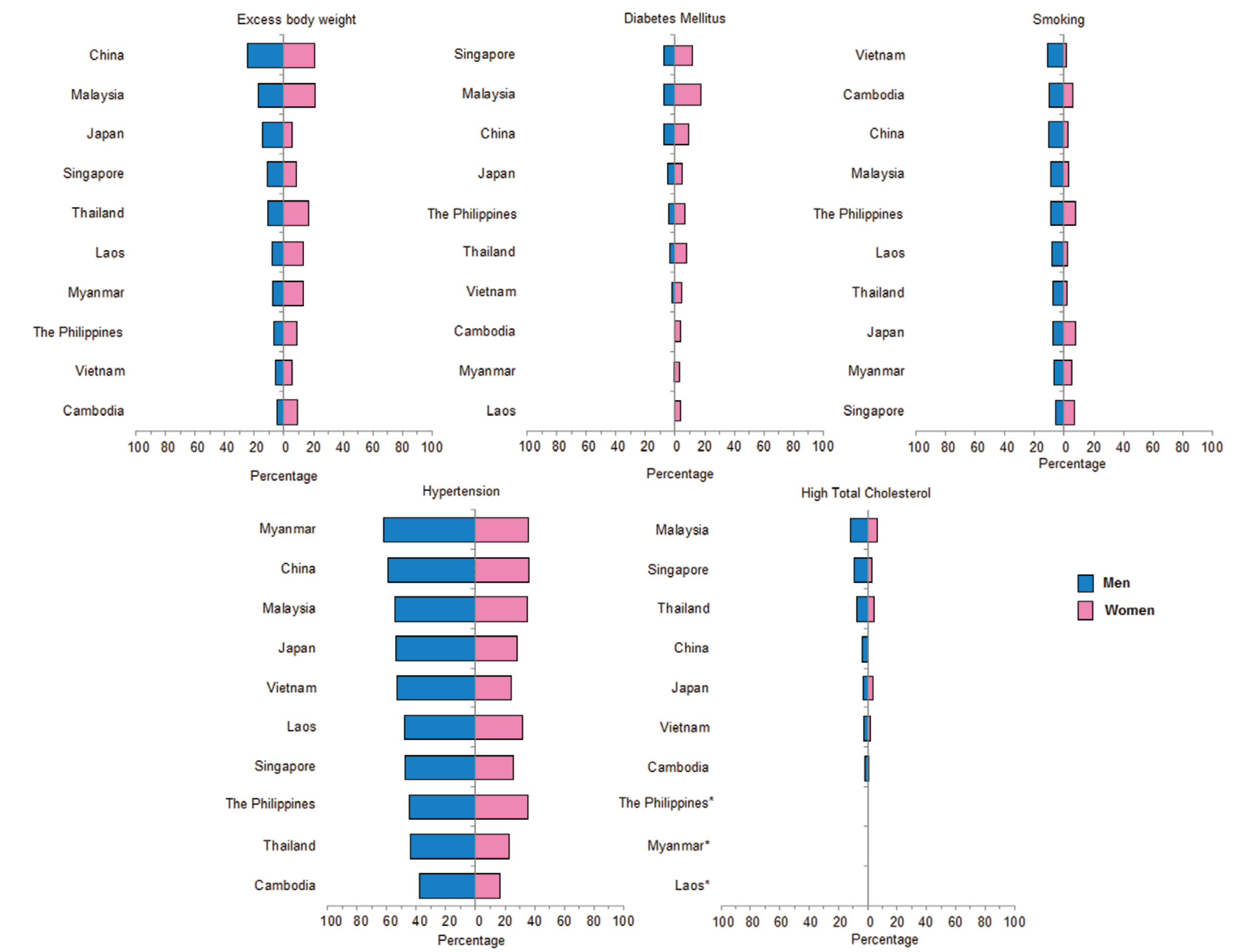

Figure 3. Population-attributable fraction (%) of all stroke explained by individual risk factors separately in men and women from selected Asian countries of the Western Pacific Region. *Information not available.

smoking prevalence rates in women tended to decline with age, suggesting a greater rate of smoking cessation in older compared with younger women.

The massive disparity in smoking prevalence rates between women and men is clearly reflected in the PAF estimates for both CAD and stroke associated with smoking, which ranged from 15% to 26% in men and from 3% to 13% in women (**Figures 2,3**). However, the disparity in the PAF estimates is somewhat attenuated by the relative risk estimates for both CAD associated with smoking being greater in women than men. Hence, despite the age-standardized smoking prevalence rate being roughly 4-fold greater in men than in women (35% vs. 9%, respectively) the PAF estimates for CAD are comparable between the sexes (15% in men vs. 13% in women).

Across age groups, the burden of smoking-related CAD in men was higher in the younger compared with the oldest age groups, a pattern that occurred in all countries with the exception of Myanmar. This reflects not only the often higher prevalence of smoking at younger ages in men, but also the stronger effect of smoking on vascular risk at younger ages. For example, in China where smoking levels were high in each age group among men (40–60%) the PAF of CAD due to smoking ranged from 30% in the 30–39-year-olds to 9% in the 60–69-year-olds. For women, the age-specific PAF estimates for CAD varied by country and were less variable than in men, partly reflecting the more constant low level of smoking among women.

Compared with CAD, smoking accounted for a smaller burden of all stroke in the Western Pacific Region, largely due to the weaker association between smoking and stroke (ie, smaller relative risks). But similar to CAD, smoking conferred a greater excess risk of stroke in women compared with men. Consequently, the sex difference in the PAF estimates for smoking and stroke were less extreme than for CAD. In men, the PAF estimates ranged from approximately 6% in Singapore to 11% in Vietnam and in women from 1% in Vietnam to 7% in Japan. Age-specific estimates of the smoking-related burden of stroke again varied both within and between countries, but as with CAD, they tended to be greater in the younger compared with older age groups for similar reasons to those outlined for CAD.

Excess Body Weight

As a result of the scale of the obesity epidemic, which is endemic in most regions of the world, with the exception of Sub-Saharan Africa, excess body weight has been identified as having the potential to threaten the substantial gains in life expectancy in the 21st century.[29] Overweight/obesity is ranked as the fifth leading cause of global mortality, causing an estimated 2.8 million deaths annually (4.8% of all deaths worldwide).[9] Although less extreme than in North America, Europe and Australia, where up to two-thirds of adults are overweight or obese, the prevalence of overweight and obesity across several countries in the Western Pacific Region (especially the most economically developed countries) is catching up to their Western counterparts, especially in women. Current estimates of the age-standardized prevalence of overweight and obesity (BMI ≥25 kg/m^2) in men ranged from 12% in Cambodia to more than 45% in Malaysia and Singapore (**Figure 1**). In China, the estimate was similar, at 43% using a lower BMI cut-point (BMI ≥24 kg/m^2) to define overweight. In women, the age-adjusted prevalence ranged from 11% in Vietnam to 51% in Malaysia, and in China it was 42% (but again with the caveat that the cut-point that was used for defining overweight was 24 kg/m^2). Within countries, and as expected, the prevalence of overweight and obesity was higher across successive age groups (**Table 3**).

The substantial variation in prevalence rates of overweight and obesity between countries is reflected by the range of PAF values for CAD attributable to the condition. The effect of BMI on the risk of CAD is equivalent in men and women, and hence the PAF estimates are comparable between the sexes (**Figure 2**). In men, estimates varied from 8% in Cambodia to 26% in Malaysia. In China, the PAF estimate was 33%, but would have been slightly lower if the same BMI definition for defining overweight and obesity had been applied. In women, the estimates ranged from 4% in Japan to 31% in Malaysia (and 29% in China). Although the prevalence of overweight and obesity increases with age, the attenuation in the strength of the association between excess weight and coronary risk partly accounts for the observed progressively smaller contribution of overweight and obesity to the burden of CAD that

Table 2. Age- and Sex-Stratified Prevalence of Cigarette Smoking and the PAF (%) of CAD and Stroke Across Selected Countries From the Western Pacific Region

Age group (years)	Men			Women		
	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)
Thailand						
15–29	34.20	5.80	26.44	0.56	1.24	1.78
30–44	41.13	7.96	22.81	1.38	1.73	2.95
45–59	42.60	9.33	15.77	2.93	1.74	4.05
60+	30.58	7.88	4.78	3.68	0.20	2.72
Japan						
20–29	37.60	4.44	19.67	12.3	33.43	42.75
30–39	43.20	6.73	21.00	11.9	32.63	44.86
40–49	43.20	9.26	20.23	12.7	28.57	44.36
50–59	41.00	11.99	17.65	11.9	21.44	41.89
60–69	31.90	14.89	13.25	8	10.75	37.58
70+	16.90	17.90	6.81	2.9	0.00	31.25
Malaysia						
25–34	49.70	8.88	30.10	2.20	3.56	5.49
35–44	50.50	9.85	24.96	3.90	4.19	7.35
45–54	41.60	8.98	16.47	1.90	1.28	2.83
55–64	36.50	8.62	10.16	5.20	1.70	5.46
Cambodia						
25–34	45.10	8.12	28.09	4.10	6.44	9.77
35–44	59.70	11.44	28.22	6.30	6.60	11.37
45–54	56.80	11.87	21.21	7.40	4.80	10.17
55–64	63.10	14.02	16.36	7.70	2.49	7.87
Myanmar						
15–24	34.70	5.75	27.63	1.00	2.33	3.26
25–34	47.50	8.52	29.15	3.30	5.25	8.02
35–44	44.50	8.79	22.66	6.20	6.50	11.20
45–54	49.50	10.51	19.00	11.60	7.32	15.08
55–64	44.00	10.21	12.00	16.80	5.28	15.71
Singapore						
18–29	28.30	4.74	23.74	8.90	17.48	23.06
30–39	32.50	6.28	19.79	5.50	7.07	11.33
40–49	29.90	6.35	14.42	5.00	4.25	8.14
50–59	22.90	5.37	8.19	2.00	0.98	2.55
60–69	23.10	5.85	5.15	1.20	0.22	1.10

(Table 2 continued the next page.)

Age group (years)	Men			Women		
	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)
The Philippines						
20–29	45.00	7.72	30.60	6.20	11.08	15.63
30–39	48.10	9.02	26.75	6.70	8.49	13.47
40–49	47.60	9.74	21.15	7.40	6.17	11.59
50–59	44.30	9.89	14.72	9.10	4.32	10.66
60–69	38.20	9.32	8.23	11.10	2.02	9.32
70+	25.10	6.80	2.39	13.20	0.00	7.41
China						
18–24	44.10	7.20	32.66	1.00	32.26	3.26
25–29	49.90	8.66	31.78	1.40	33.58	3.83
30–34	54.80	9.88	31.08	1.70	33.25	4.09
35–39	58.50	10.95	29.59	1.90	32.06	4.02
40–44	58.90	11.50	26.75	2.00	30.10	3.71
45–49	59.70	12.12	23.94	2.40	27.39	3.86
50–54	60.30	12.71	20.95	2.70	23.92	3.74
55–59	56.60	12.48	16.82	3.60	19.62	4.23
60–64	51.60	11.93	12.60	4.00	14.39	3.97
65–69	49.50	11.92	9.26	4.90	8.09	4.03
70+	40.10	10.44	3.76	5.80	0.00	3.40
Vietnam						
25–34	53.00	9.41	20.63	0.70	1.16	44.20
35–44	61.90	11.81	20.85	1.30	1.44	44.88
45–54	56.00	11.73	19.16	2.30	1.54	43.35
55–64	53.30	12.10	15.68	4.10	1.34	39.97
Laos						
25–34	30.70	5.68	21.01	1.10	1.81	2.82
35–44	43.90	8.68	22.43	2.00	2.19	3.91
45–54	51.60	10.91	19.65	2.40	1.61	3.54
55–64	43.30	10.06	11.83	2.90	0.95	3.12

CAD, coronary artery disease; PAF, population-attributable fractions.

occurs with age.

The relationship between overweight and obesity is weaker for all stroke than it is for CAD, but broadly consistent between women and men. Hence, the PAF estimates for stroke attributable to the condition were smaller than with CAD in both sexes (**Figure 3**). In men, the age-standardized PAF estimates ranged from 5% in Cambodia to 17% in Malaysia (and 25% in China using the lower BMI criterion for defining overweight). In women, the estimates ranged from 5% in Vietnam and Japan to 22% in Malaysia (and 21% in China). As with CAD, the relationship between excess weight and stroke risk attenuates with age, which is reflected in the smaller proportion of all strokes explained by overweight and obesity across successive age groups.

Diabetes

Perhaps the most significant global health effect resulting from the growing obesity pandemic has been the rapid increase in the prevalence of type 2 DM. Currently, there are an estimated 350 million individuals worldwide living with DM, approximately 40% of whom live in the Western Pacific Region.[30] Based on current patterns, the overall global prevalence is projected to increase to 438 million within the next 15 years.[30] And again, as with CVD, a disproportionate amount of the burden will fall on those lower- and middle-income countries in the Western Pacific Region. High blood glucose is ranked as the third leading cause of global mortality behind BP and tobacco use, and is responsible for 3.4 million deaths annually (5.8% of all deaths).[9]

In men, the age-standardized prevalence ranged from roughly 1% in the least-developed countries such as Cambodia and Myanmar to approximately 11–12% in Japan, Singapore and China (**Figure 1**). However, it is important to note that in Cambodia and Myanmar, the prevalence of DM was based on a previous diagnosis; however, approximately 80% of the study population from those 2 countries had never undergone a medical examination, so estimates for the prevalence of DM are likely to be gross underestimates (the International Diabetes Federation estimates the prevalence of diabetes in adults aged 20–79 years to be 2.6% in Cambodia and 6.1 years in Myanmar). Given the strong effect of aging on the risk of DM, it is not surprising that prevalence was observed to be higher in successive age groups (**Table 4**). But, what is of particular concern was that the prevalence of DM in men under 50 years is alarmingly high: in Singapore the prevalence of DM in men aged 40–49 years was over 13% and was 16% in men aged 45–54 years in Malaysia, supporting previous observations that Asians are at increased risk of developing DM at younger ages compared with non-Asians. In women, the age-standardized prevalence rates were not too dissimilar from those of men and ranged from approximately 2% in Cambodia and Myanmar to 11% in China and 13% in Malaysia. As with men, the age-specific prevalence rates were higher at older ages, with evidence in some countries of notably high rates in

Table 3. Age- and Sex-Stratified Prevalence of Excess Body Weight and the PAF (%) of CAD and Stroke Across Selected Countries From the Western Pacific Region

Age group (years)	Men			Women		
	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)
Thailand						
15–29	18.53	12.99	19.67	20.63	15.79	25.06
30–44	32.2	14.87	22.27	44.19	21.66	31.34
45–59	33.75	9.69	15.38	50.64	16.30	22.61
60+	22.18	1.98	4.29	36.15	4.88	5.55
Japan						
20–29	15.2	18.48	15.73	7.80	6.21	5.52
30–39	28	23.60	20.88	12.10	7.41	6.51
40–49	36.6	22.11	20.24	16.20	7.39	6.35
50–59	31.6	13.62	13.09	21.60	6.86	5.65
60–69	29.6	7.28	7.84	22.80	4.46	3.31
70+	27.3	1.83	3.24	24.60	1.99	0.87
Malaysia						
25–34	46.1	23.33	33.24	45.40	25.46	36.91
35–44	33.6	14.26	21.47	54.90	23.97	33.85
45–54	55.1	16.01	24.26	54.30	18.37	25.53
55–64	50	9.58	15.93	53.60	12.68	16.81
Cambodia						
25–34	7.7	4.84	7.68	12.00	8.28	13.39
35–44	12.6	5.87	9.30	23.00	11.67	17.66
45–54	14.7	4.84	7.87	24.10	9.08	13.20
55–64	16.2	3.32	5.78	20.40	5.24	7.14
Myanmar						
15–24	7.5	5.95	9.41	9.70	8.44	14.24
25–34	13.5	8.18	12.73	23.40	14.97	23.17
35–44	21.9	9.78	15.12	37.80	17.84	26.06
45–54	23.3	7.46	11.93	39.70	14.13	20.04
55–64	18.6	3.79	6.58	31.60	7.89	10.65
Singapore						
18–29	15.4	28.87	46.83	5.80	5.82	10.20
30–39	16.1	22.80	34.45	8.70	7.04	10.84
40–49	10.3	12.61	18.12	11.10	7.69	10.74
50–59	9.8	9.21	11.50	13.20	7.77	9.68
60–69	5.7	3.96	3.93	8.70	4.43	4.77
The Philippines						
20+	27.6	7.03	12.20	34.40	8.59	10.11
China						
18–24	41.6	27.89	35.97	33.50	19.43	27.91
25–29	48.9	24.85	33.11	54.90	24.44	33.05
30–34	40.6	15.61	22.68	48.90	18.65	24.78
Vietnam						
25–34	12.8	7.79	12.15	6.90	4.93	8.17
35–44	11.9	5.56	8.83	10.00	5.43	8.53
45–54	13.3	4.40	7.18	16.40	6.37	9.38
55–64	11.6	2.40	4.21	17.90	4.63	6.32
Laos						
25–34	9.9	6.14	9.66	17.70	11.75	18.57
35–44	26.4	11.55	17.68	32.60	15.77	23.31
45–54	25.2	8.02	12.78	36.90	13.27	18.89
55–64	35.1	6.92	11.74	36.66	9.04	12.15

CAD, coronary artery disease; PAF, population-attributable fractions.

Table 4. Age- and Sex-Stratified Prevalence of Diabetes and the PAF (%) of CAD and Stroke Across Selected Countries From the Western Pacific Region

Age group (years)	Men			Women		
	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)
Thailand						
15–29	0.79	1.20	2.24	0.49	1.80	0.68
30–44	3.68	3.84	6.18	3.20	6.93	4.01
45–59	8.49	5.76	7.81	11.55	13.36	12.26
60+	13.79	4.76	4.44	17.61	8.48	16.21
Japan						
20–29	0.60	0.86	1.56	0.00	0.00	0.00
30–39	1.40	1.57	2.62	1.10	2.66	1.43
40–49	5.40	4.55	6.73	1.70	2.90	2.09
50–59	12.20	7.39	9.58	6.20	6.79	6.87
60–69	20.70	8.59	9.29	12.60	8.29	12.45
70+	23.20	6.05	4.34	16.70	5.61	15.15
Malaysia						
25–34	6.50	7.71	12.83	4.90	12.54	6.21
35–44	4.50	4.34	6.76	8.70	15.45	10.06
45–54	16.30	11.08	15.07	20.80	23.14	20.26
55–64	20.20	10.01	11.94	28.20	20.82	24.64
Cambodia						
25–34	0.30	0.38	0.67	0.60	1.73	0.80
35–44	0.20	0.20	0.32	1.30	2.66	1.64
45–54	3.10	2.32	3.27	4.20	5.73	4.88
55–64	3.50	1.89	2.29	5.90	5.22	6.40
Myanmar						
15–24	0.00	0.00	0.00	0.40	1.56	0.56
25–34	0.00	0.00	0.00	0.70	2.01	0.94
35–44	2.00	1.98	3.12	1.80	3.64	2.26
45–54	1.80	1.36	1.92	3.10	4.29	3.65
55–64	4.10	2.21	2.68	4.30	3.86	4.75
Singapore						
18–29	0.60	0.95	1.81	1.30	4.91	1.81
30–39	5.90	6.31	10.17	2.80	6.51	3.56
40–49	13.30	10.50	15.08	11.00	16.18	12.12
50–59	23.70	13.42	17.07	15.00	14.98	15.15
60–69	24.10	9.86	10.65	33.40	19.33	27.38
The Philippines						
20–29	1.30	1.83	3.33	0.80	2.66	1.10
30–39	3.40	3.74	6.13	2.80	6.51	3.56
40–49	7.10	5.90	8.66	5.60	8.95	6.56
50–59	10.20	6.26	8.14	10.80	11.26	11.39
60–69	12.10	5.20	5.65	12.90	8.47	12.71
70+	7.80	2.12	1.50	8.70	3.00	8.51
China						
18+	12.10	7.42	9.50	11.00	9.24	11.85
Vietnam						
25–34	2.00	2.51	4.33	0.70	2.01	0.94
35–44	1.50	1.49	2.36	1.70	3.45	2.14
45–54	4.10	3.04	4.27	3.60	4.95	4.21
55–64	0.060	3.20	3.87	7.90	6.86	8.39
Laos						
25–34	0.000	0.00	0.00	0.10	0.29	0.14
35–44	0.005	0.50	0.80	2.20	4.42	2.75
45–54	0.027	2.02	2.86	4.50	6.12	5.21
55–64	0.033	1.79	2.17	8.80	7.58	9.26

CAD, coronary artery disease; PAF, population-attributable fractions.

Table 5. Age- and Sex-Stratified Prevalence of High Cholesterol and the PAF (%) of CAD and Stroke Across Selected Countries From the Western Pacific Region

Age group (years)	Men			Women		
	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)	Prevalence (%)	Stroke PAF (%)	CAD PAF (%)
Thailand						
15–29	7.37	8.89	17.07	10.35	0.44	14.29
30–44	19.91	12.19	24.86	15.76	1.97	13.77
45–59	24.82	5.61	17.70	36.12	7.35	16.62
60+	26.82	0.00	5.56	42.51	12.64	5.45
Japan						
20–29	2.10	2.42	5.05	4.90	0.29	6.76
30–39	10.90	7.74	16.33	5.80	0.67	5.92
40–49	13.80	5.67	14.23	10.60	1.83	7.38
50–59	15.10	2.42	10.04	24.30	5.49	10.31
60–69	10.70	0.00	3.83	21.50	6.17	4.88
70+	6.10	0.00	0.51	11.80	4.25	0.48
Malaysia						
25–34	41.30	15.24	39.04	39.60	3.02	30.42
35–44	52.60	13.44	38.87	56.80	6.01	32.05
45–54	61.60	9.43	36.00	63.20	8.54	27.23
55–64	72.00	3.80	32.11	71.30	11.60	21.53
Cambodia						
25–34	0.90	0.86	1.89	1.20	0.10	1.50
35–44	2.70	1.58	3.84	2.40	0.35	2.14
45–54	3.90	1.13	3.60	6.60	1.35	3.85
55–64	4.70	0.23	2.50	10.00	2.65	3.39
Singapore						
18–29	12.00	14.59	26.33	4.90	0.15	7.70
30–39	21.20	14.03	27.51	10.70	1.22	10.39
40–49	18.50	7.45	18.20	17.50	2.99	11.63
50–59	19.80	3.15	12.76	30.90	6.88	12.75
60–69	22.90	0.00	7.86	23.70	6.76	5.35
China						
18–44	3.00	3.50	7.56	1.30	0.21	1.62
45–59	4.50	3.42	7.94	5.00	0.97	4.54
60+	2.90	1.27	3.59	6.90	1.58	4.49
Vietnam						
25–34	2.90	2.72	5.84	1.40	0.12	1.75
35–44	4.70	2.72	6.50	3.70	0.54	3.26
45–54	6.80	1.95	6.11	9.90	2.01	5.66
55–64	6.60	0.32	3.47	13.20	3.47	4.42

CAD, coronary artery disease; PAF, population-attributable fractions.

women under 50 years of age.

Across the region, there was a 10-fold variation in the burden of CAD attributable to DM in men: the lowest age-standardized PAFs occurred in Cambodia, Laos and Myanmar, where only approximately 1% of all CAD was attributable to DM, whereas up to 12% of CAD in Malaysian men could be explained by DM (**Figure 2**). In China, approximately 10% of all CAD in men was attributable to DM. The age-specific PAF estimates revealed an interesting pattern apparent in most of the countries, that of an inverse U-shaped relation in the burden of CAD attributable to DM with age: estimates of the PAF tended to increase up to around the age of 60 years in men where they then plateaued and subsequently declined in older age groups, a likely consequence of the often sizeable attenuation in the strength of the association between DM and incident CAD with age. In women, although age-specific prevalence rates for DM were often considerably less than for men, the PAF estimates for CAD were often higher due to the greater excess coronary risk that DM confers in women compared with men. This is most apparent in Japan where the prevalence of DM in every age group, and hence the overall prevalence was notably less in women than in men (8% vs. 11%), yet the overall PAF estimate was slightly higher in women compared with men (7.4% vs. 5.8%). Across countries, the burden of CAD attributable to DM in women varied from 2–3% in Laos, Cambodia and Myanmar to 12–13% in China and Malaysia.

In men, depending on the country, the strength of the association between DM and risk of all strokes tended to be weaker in magnitude to that for CAD but, as with CAD, showed substantial attenuation with age (**Table 4**). Hence, DM tended to account for a lesser burden of all stroke in men than CAD and ranged from less than 1% in Myanmar and Cambodia to

7–8% in China, Singapore and Malaysia. In women, relative risks for the association between DM and all stroke tended to be higher than with CAD, especially at younger ages, and as with CAD were greater than for men. Hence, DM accounted for a higher burden of all strokes than for CAD in many of the countries, including The Philippines (6%), Thailand (7%), Singapore (11%) and Malaysia (17%), but not Japan (5%) or China (9%, although it was not possible to calculate age-specific effects) (**Figure 3**).

Hypercholesterolemia

Elevated TC level is considered to be the 6th leading cause of the global burden of mortality, accounting for 4.5% of all deaths annually.[9] Obesity, poor diet, and low levels of physical activity are all risk factors associated with high cholesterol levels. It is therefore unsurprising for countries that have experienced substantive changes in the proportion of its population transitioning from an agrarian to a more industrialized existence (in addition to very low usage at the population level of lipid-lowering agents) to have a high prevalence of hypercholesterolemia. Of the 10 countries surveyed, 7 had age-standardized prevalence estimates for hypercholesterolemia, with the highest rates occurring in Malaysia (approximately 53% in women and men, although it should be noted that the cut-point for hypercholesterolemia in Malaysia was lower at 5.2 mmol/L compared with the more usual definition of 6.2 mmol/L) and Thailand (19% in men and 24% in women). In contrast, China, Cambodia and Vietnam all had low levels of hypercholesterolemia, with only 3–6% of the population affected (**Figure 1**). Irrespective of the country, the prevalence of hypercholesterolemia increased across age groups in both sexes (**Table 5**).

Driven by the sizeable variation in population prevalence estimates for hypercholesterolemia, the PAF estimates for CAD associated with the condition varied enormously between countries. In Singapore, 20% of all CAD in men and 10% in women could be attributed to TC levels >6.2 mmol/L, whereas in Malaysia the corresponding estimates were 37% and 29%, respectively (although not directly comparable with other countries due to the lower cut-point for TC used to define hypercholesterolemia). By comparison, less than 3% of all CAD in Cambodia could be attributed to hypercholesterolemia and in China, 7% of CAD in men and 3% in women could be explained by the condition (**Figure 2**). As with BP and DM, there was attenuation in the association with age such that the effect of high cholesterol levels on CAD became progressively smaller in older age groups (**Table 5**).

The relationship between TC and all strokes is clouded by the opposing associations between TC and the major stroke subtypes.[31] For ischemic stroke the relationship with TC is positive, whereas with hemorrhagic stroke (which is much more common in Asian compared with non-Asian populations[32]) the association is weakly inverse. Consequently, the PAF estimates for all strokes due to hypercholesterolemia are dependent, in part, on the proportion of all strokes that are ischemic or hemorrhagic in origin, as well as the age-structure of the population. So for example, in Malaysia, 12% of all strokes in men and 6% in women can be explained by high cholesterol, and in Singapore the corresponding estimates are 9% and 3%, respectively (**Figure 3**). By comparison, in China, the corresponding estimates are substantially less at 3% and 0.6%, respectively, reflecting both the low prevalence of the condition as well as a greater proportion of hemorrhagic vs. ischemic strokes in the Chinese population.

Conclusions

The 10 most populous Asian countries that comprise the Western Pacific Region represent an economically, socially and culturally diverse constellation of countries. And yet, despite the considerable heterogeneity that exists both within and between these populations, they are united by the huge and growing burden of CVD that is common to them all – although to a variable extent. Irrespective of the country, the 5 modifiable risk factors that were selected for this review could explain a substantial proportion of all CAD and strokes in men and women at all ages. As a single risk factor, hypertension was preeminent across all countries in its ability to explain the greatest proportion of all CAD and strokes in the population, reaffirming the need to reprioritize the global management and control of BP within populations.[33] Moreover, it is likely that the PAF estimates for hypertension (as well as for the other continuous risk factors that were categorized ie, cholesterol, blood glucose and body weight) underestimated the true burden of vascular disease due to suboptimal BP (as opposed to ‘hypertension’) given the log-linear nature of the relation between BP and vascular outcomes.[34]

As highlighted by the data, there was considerable variation in the burden of vascular disease across age and sex groups depending on the risk factor in question. Hence, the anticipated benefits in terms of CVD prevention as a consequence of the effective implementation of either primary prevention programs (such as population-wide salt-reduction strategies[35]) or secondary prevention programs (including, for example, the treatment of individuals at high risk with BP- or cholesterol-lowering medication)[36] would differ across population subgroups. Such information could prove useful when it comes to planning primary and secondary cardiovascular preventive strategies. For example, cigarette smoking in particular, was responsible for a far greater burden of vascular disease in men than in women, particularly in the younger age groups. Thus, in addition to population-wide policies (such as raising taxes on cigarettes) the implementation of smoking cessation strategies specifically tailored towards young Asian men may reap greater benefits than more generic smoking cessation campaigns. In contrast, population-wide measures to reduce BP levels would be similarly beneficial in women and men, old and young. When funds are limited, knowing which risk factor to target in which subgroup of the population and with what intervention so as to derive maximal benefit, is crucial for any informed decision making process.

Conflict of Interest Statement

Mark Woodward has served as a consultant to Novartis and Sanofi and as a consultant to Amgen.

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Supplementary Files

Supplementary File 1

Table S1. Major causes of death in China (%), 1957–2000

Table S2. Characteristics of studies included in the present analysis of the age- and sex-specific burden of cardiovascular disease attributable to 5 major and modifiable risk factors in 10 Asian countries of the Western Pacific Region

Figure S1. Proportion of mortality attributed to selected diseases and injuries in 10 countries of the Western Pacific Region.

Please find supplementary file(s);
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